

## The Incidence and Characteristic of Acute Kidney Injury as A Complication of Severe Burn Injury in Patients Receiving Fluid Resuscitation

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**Background:** Acute kidney injury is important factor that can increase mortality in patient with severe burn injury. Knowledge about incidence and characteristic of acute kidney injury among severe burned patients will help medical practitioner to establish appropriate medical decision and health care protocol.

**Method:** PubMed, Cochrane Library, and Google™ search yielded 12 articles. The articles were screened by inclusion criteria, exclusion criteria, and full text reading. Five remaining articles appraised in regard of validity, importance, and applicability.

**Result:** Incidence of acute kidney injury among severely burned patients varies from 24.4% to 53.3%. According to the study with best level of evidence, a systematic review, the incidence of AKI is 28.8% (95% CI 26.8%-30.7%). AKI can occur early or late, and may progress. Progressive AKI has highest mortality rate.

**Conclusion:** AKI is common complication among patients with severe burn injury. Approximately one-third to half of patients with severe burn injury will develop AKI in the course of the disease. Early clinical assessment and re-evaluation are important in severe burn injury management.

**Keywords:** *Acute kidney injury, burns, prognosis*

**Latar Belakang:** Gagal ginjal akut atau *acute kidney injury* (AKI) merupakan faktor penting yang dapat meningkatkan angka mortalitas pada pasien dengan luka bakar berat. Pengetahuan mengenai insiden dan karakteristik AKI pada pasien dengan luka bakar berat dapat membantu pelaku medis untuk menentukan keputusan medis dan protokol perawatan yang tepat.

**Metode:** Pencarian pada PubMed, Cochrane Library, and Google™ menghasilkan 12 artikel. Artikel-artikel tersebut diseleksi berdasarkan kriteria inklusi, kriteria eksklusi, dan pembacaan artikel secara utuh. Penelaahan kritis pada aspek *validity, importance, dan applicability* dilakukan terhadap 5 artikel yang terpilih.

**Hasil:** Insiden gagal ginjal akut pada pasien dengan luka bakar berat bervariasi dari 24.4% hingga 53.3%. Berdasarkan studi dengan *level of evidence* yang tertinggi, sebuah *systematic review*, insiden AKI adalah 28.8% (95% CI 26.8%-30.7%). AKI dapat muncul awal atau terlambat, dan dapat mengalami progresivitas. AKI yang progresif memiliki angka mortalitas paling tinggi.

**Kesimpulan:** AKI merupakan komplikasi yang umum pada pasien dengan luka bakar berat. Sekitar sepertiga hingga setengah pasien dengan luka bakar berat akan mengalami AKI dalam proses perjalanan penyakitnya. Pemeriksaan klinis dini dan evaluasi ulang sangat penting dalam manajemen luka bakar berat.

**Kata Kunci:** *Acute kidney injury, burns, prognosis*

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**A**cute kidney injury (AKI) is the most common complication in patient with severe burn injury and can increase mortality rate.<sup>1-6</sup> Severe burn injury can be defined as acute burn injury that needs

specialized care during admission.<sup>7</sup> At present, RIFLE (Risk, Injury, Failure, Loss of function, and End stage kidney disease) classification, which was modified into staging system, is used to diagnose and classify AKI.<sup>2,3</sup> In current

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medical practice, most patients with severe burn injury survive early resuscitation. However, AKI associated with other organ dysfunction become one of the major causes of death in those patients.<sup>4</sup> Knowledge about the incidence and characteristic of AKI among patients with severe burn injury will aid physicians to establish appropriate medical decisions and health care protocol.

## METHODS

A PubMed search was performed on 27<sup>th</sup> December 2012. The author used following Medical Subject Headings or MeSH terms: “severe burn injury”, and in refining order

“acute kidney injury”, “acute renal failure” and “acute renal insufficiency”. (Table 1) Search results were limited to English, human, and adult population studies. Cochrane Library and Google™ search engine were also used to discover relevant articles.

Studies about adult populations with severe burn injury, providing epidemiologic data on incidence of acute kidney injury were included. Studies that explored different outcome, conducted in intervention setting, or pediatric population were excluded. After reading the full texts, studies that included patients with burn injury less than 20% of total body surface area (TBSA) or did not use RIFLE criteria to establish the diagnosis of AKI, were

**Table 1.** Search strategy used, conducted on 27<sup>th</sup> December 2012

Search Engine	Search Terms
<i>PubMed</i>	(severe[All Fields] AND (“burns”[MeSH Terms] OR “burns”[All Fields] OR (“burn”[All Fields] AND “injury”[All Fields]) OR “burn injury”[All Fields])) AND (“acute kidney injury”[MeSH Terms] OR (“acute”[All Fields] AND “kidney”[All Fields] AND “injury”[All Fields]) OR “acute kidney injury”[All Fields]) OR (“acute kidney injury”[MeSH Terms] OR (“acute”[All Fields] AND “kidney”[All Fields] AND “injury”[All Fields]) OR “acute kidney injury”[All Fields]) OR (“acute”[All Fields] AND “renal”[All Fields] AND “failure”[All Fields]) OR “acute renal failure”[All Fields]) OR (“acute kidney injury”[MeSH Terms] OR (“acute”[All Fields] AND “kidney”[All Fields] AND “injury”[All Fields]) OR “acute kidney injury”[All Fields]) OR (“acute”[All Fields] AND “renal”[All Fields] AND “insufficiency”[All Fields]) OR “acute renal insufficiency”[All Fields])) AND (“humans”[MeSH Terms] AND English[lang] AND “adult”[MeSH Terms])
<i>Cochrane Library</i>	burn injury, acute kidney injury, acute renal failure, acute renal insufficiency, prognosis
<i>Google™</i>	burn injury, acute kidney injury, acute renal failure, acute renal insufficiency, prognosis

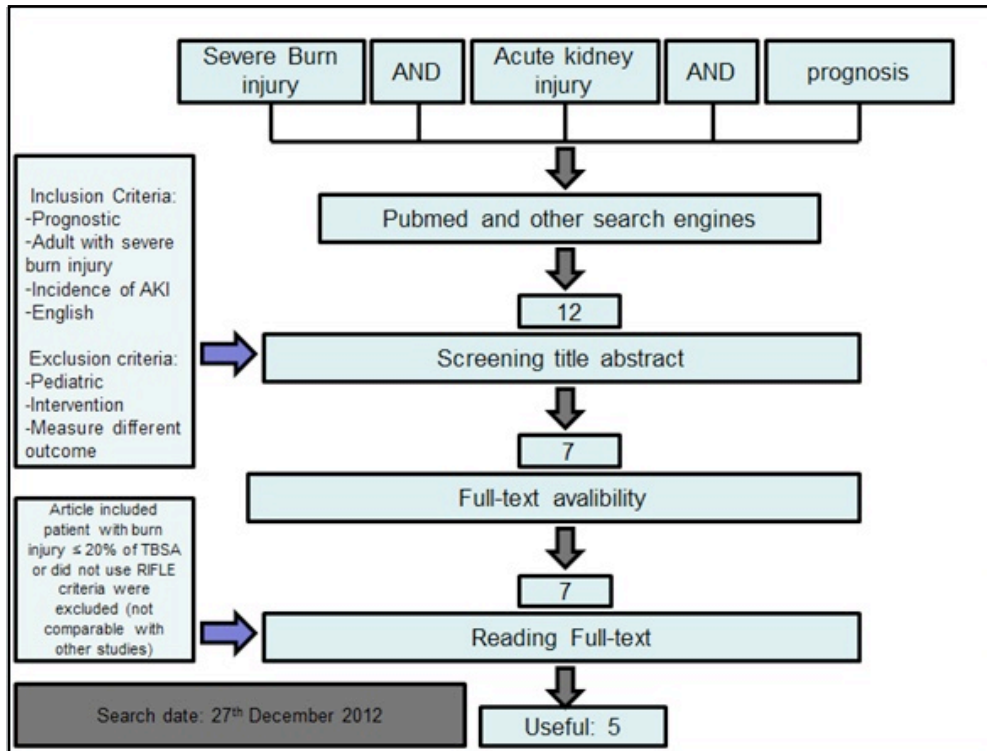


Figure 1 . Flow chart of conducted selection process

excluded because they are not comparable with other studies. (Figure 1)

## RESULTS

The appraised articles are cohort studies and a systematic review, thus they regarded as high-level evidences. The critical appraisal of the articles is shown in Figure 2 and Figure 3. Palmieri et al, Steinvall et al, Mosier et al, and Schneider et al included patients older than 18 years old with burn injury more than 20% of TBSA that received fluid resuscitation therapy. The diagnosis criteria used in those studies were RIFLE criteria developed by Acute Dialysis Quality Initiative Group. Systematic review, conducted by Brusselaers et al, included 57 publications with varying diagnosis criteria, but it described a sub-group that used RIFLE criteria.

Palmieri et al studied 60 consecutive patients that were admitted to University of California Davis Burn ICU over 2 years period. The study design was retrospective cohort .The incidence of AKI was 53.3% (95%CI 40.1%-66.1%). They used the earliest available

creatinine serum concentration as baseline creatinine level of RIFLE criteria. Patients with AKI had higher mortality rate than patients without AKI while patients with progressive AKI associated with higher mortality rate.<sup>3</sup>

Steinvall et al studied 127 patients consecutively admitted to a national burn centre in 8.5 years. The study design was prospective cohort study. Incidence of acute kidney injury was 24.4% (95 CI 17.4%-32.9%). They also used earliest available creatinine serum concentration as baseline creatinine level. They classify the occurrence of AKI into two groups, which are early (within first week) and late (within 8-60 days).<sup>4</sup>

Mosier et al used a retrospective review of patients enrolled in the prospective observational multicenter study. Among 221 patients, 62 patients met AKI criteria within 24 hours (during resuscitation phase), while 47 patients developed AKI later. The incidence of AKI was 49.3% (95 CI 42.5%-56.0%). This study used estimated creatinine serum concentration based on age, sex, and race, as baseline creatinine level. Patients developed progressive



Criterion*	Validity					Importancy		Applicability		Level of Evidence***
	Patients assembled at a common point of disease	Follow up sufficiently long and complete	Blinding	Adjustment for important prognostic factors	Validation in an independent group	Outcome over time**	Precision of prognostic estimates (95% CI)	Patient similarity	Important impact on patient	
Steinval <i>et al</i>	+	+	-	+	-	24.4%	17.4–32.9%	+/-	+	I
Mosier <i>et al</i>	+	+	-	+	-	49.3%	42.5–56.0%	+/-	+	I
Palmieri <i>et al</i>	+	+	-	+	-	53.3%	40.1–66.1%	+/-	+	I
Schneider <i>et al</i>	+	+	-	+	+	47.0%	40.5–53.6%	+/-	+	I

\* (+): yes/achieved; (-): no/not achieved; (+/-): somewhat achieved; 95% CI calculated using Wilson formula

\*\* Outcome measured was acute kidney injury according to RIFLE criteria

\*\*\* Level of evidence obtained from American Society of Plastic Surgeon Evidence Rating Scales (available at <http://www.plasticsurgery.org>) (Appendix)

Figure 2 . Critical appraisal of articles based on its validity, importancy, and applicability

Criterion*	Validity			Importancy		Applicability		Level of Evidence***
	Systematic review of high quality studies which are relevant to question	Method section adequately describe how all relevant studies were found and assessed	Consistency of studies (clinically and statically)	Outcome over time**	Precision of prognostic estimates (95% CI)	Patient similarity	Important impact on patient	
Brusselsaers <i>et al</i>	+	+	-	28.8%	26.8–30.7%	+/-	+	I

\* (+): yes/achieved; (-): no/not achieved; (+/-): somewhat achieved; 95% CI calculated using Wilson formula

\*\* Outcome measured was acute kidney injury according to RIFLE criteria

\*\*\* Level of evidence obtained from American Society of Plastic Surgeon Evidence Rating Scales (available at <http://www.plasticsurgery.org>) (Appendix)

Figure 3 . Critical appraisal of systematic review based on its validity, importancy, and applicability

AKI had the highest mortality rate compared to early and late developed AKI.<sup>5</sup>

Schneider et al used the same study population as Mosier et al. Consequently, epidemiologic and mortality profile of patient groups (early, late, progressing AKI) between the two studies are similar. The incidence of AKI was 47% (95 CI 40.5%-53.6%). However, Schneider et al added an interesting classification and regression tree (CART) analysis that describe some characteristics of patients who developed late AKI.<sup>6</sup> (Figure 4)

Brusselsaers et al conducted a systematic review covering 57 articles published between 1960 to 2009. The incidence of AKI among the studies is varying between 0.2% to 64.1%. If we only look up to a sub-group of study using RIFLE criteria, the incidence of AKI will be 28.8% (95%CI 26.8%-30.7%).<sup>1</sup>

Titles above the boxes indicate predictor variables (and appropriate limits) while the boxes contain data on how each predictor split the subjects within that group according to the outcome (Late AKI). Patients who suffered late AKI are coded as black while those not suffering late AKI are gray as indicated. AKI, acute kidney injury; NROF, non-renal organ failure score; lowest 24 hr BD, the lowest base deficit value obtained within the first 24 hours of admission; lowest 24 hr glucose, the lowest glucose value obtained within the first 24 hours of admission.

### DISCUSSION

Studies conducted by Steinvall et al, Mosier et al, Schneider et al, and Palmieri et al have good level of validity as blinding is not of great value in such studies. The similar patient inclusion and diagnosis criteria result in

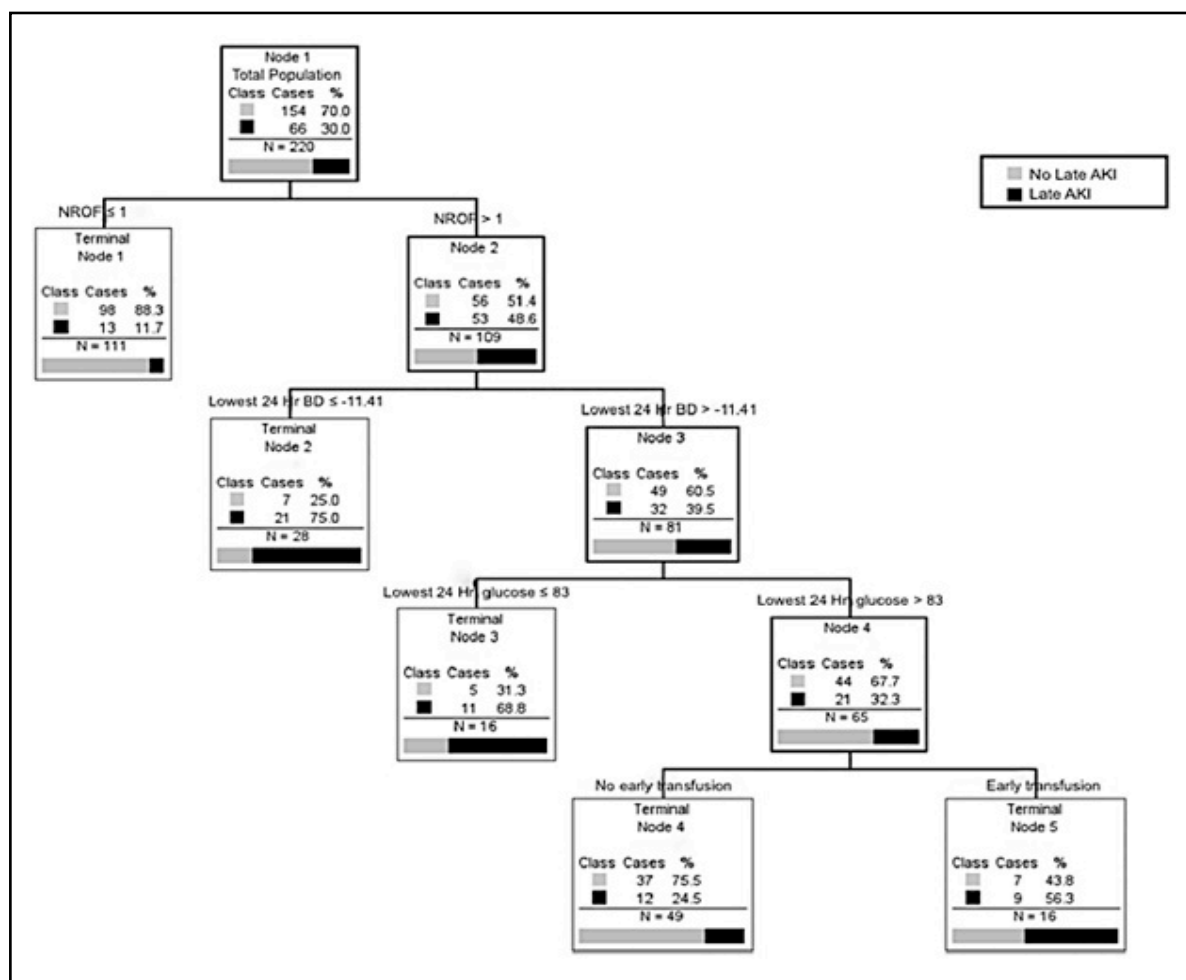


Figure 4 . Classification and Regression Tree (CART) analysis to predict late AKI

comparable importance. However, those studies show varying incidence of AKI (24.4% to 53.3%).

One of the most important factors that might cause such variation is the difficulty to obtain accurate base creatinine level. The diagnosis of AKI using RIFLE criteria is best achieved when the individual base level of serum creatinine had been acquired before the insult that lead to AKI occurred. In the case of burn injury, it is almost impossible to get patient's base creatinine level prior to the injury. This causes disagreement between the studies to determine the base level of patient's creatinine serum concentration. Some opted to take the first available creatinine serum concentration during admission, while the others chose to use estimated creatinine serum concentration based on demographic profile. The decision to use first available creatinine serum concentration might cause underestimation of AKI incidence because the creatinine serum level obtained at the time of admission may already increase during the interval between the burn injury occurrence and the blood laboratory analysis. On the other hand, estimated creatinine serum concentration might not be accurate. Other differences between the studies that may influence the outcome are slight differences of population baseline characteristics and treatment protocol. Muscle injury can also increase creatinine serum level, therefore it can cause over estimation of AKI.<sup>1</sup>

Patients enrolled in those studies are mostly Caucasian and have mean age of around 40 years old.<sup>3-6</sup> These demographic factors can reduce the applicability of the studies to our case, or Indonesian patients in general. In applicability aspect, Mosier et al and Schneider et al have the advantage compared to the other two cohort studies, because the study population was based on multicenter database. The systematic review conducted by Brusselaers et al also has a good validity even though the consistency of studies reviewed is not achieved. The consistency was not achieved because of differences in AKI diagnosis criteria, inclusion criteria, treatment given, and follow up period among studies reviewed. In spite of this, the study described a sub-group of studies conducted using RIFLE criteria. Hence, the importance of the study can be calculated and

compared to other studies. The systematic review has decent validity, highest level of evidence, and narrowest confidence interval compared to other studies. The 28.8% AKI incidence among severe burn injury patients in this study is considered the most reliable and applicable of all other studies due to the large number of samples from various studies. Despite the differences, all of the studies appraised, agree that AKI is a common complication among patient with severe burn injury receiving fluid replacement therapy.

Some important AKI characteristics described by the studies are its onset and progression. AKI can appear during resuscitation phase or as late as 60 days after the injury.<sup>4,6,7</sup> This fact implicates that medical providers must always be alert, because it can occur from time to time despite adequate fluid resuscitation. CART analysis of Schneider et al can help reducing the potential pitfall of overlooked AKI that occurs later than 48 hours. Patients who have multiple organ failures (non-renal), lowest base deficit below -11.41 during first 24 hours, lowest blood glucose level below 83 mg/dL during first 24 hours, and early transfusion (within first 24 hours) need to be closely monitored.<sup>6</sup> Regarding the progression, progressive AKI has a significantly higher mortality rate.<sup>3,5,6</sup> Thus, frequent re-evaluation of creatinine serum level and urine output of AKI patients are of great importance to detect progressive AKI immediately.

## CONCLUSION

Based on the results, we can conclude that, AKI is a common complication of severe burn injury regardless of adequate fluid resuscitation. The incidence of AKI in patients with severe burn injury varies considerably among studies. However, when AKI is defined by the RIFLE consensus classification, it occurs in around one-third to half of patients with severe burn injury. The important characteristics of AKI that needs great consideration are the onset that can be early or late, and the high mortality rate of progressing AKI. Early obtained and re-evaluation of important clinical data are vital in severe burn injury management. Early identification could be a key factor to reduce mortality of AKI in patients with severe burn injury.

Referring to the case presented in this study, the patient has a significant probability to develop AKI despite adequate fluid resuscitation. (Level of evidence I) Important clinical data (serum creatinine concentration, urine output, blood gas analysis (including base deficit), blood glucose concentration, markers for suspected non-renal organ failure) must be acquired as soon as possible during admission. Those data should be re-evaluated within the first 24 hours of injury. They may well be re-evaluated again later if necessary. Since AKI might develop very late during the course of the disease, the aforementioned data might be beneficial to determine the likelihood of the patient to develop late AKI. (Level of evidence I) If the patient develops AKI during hospitalization period, the probability of RIFLE class progression must be properly anticipated for its high mortality rate. (Level of evidence I).

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